(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

REMARKS

The present invention is directed to methods for the treatment of cancer, comprising administration of a composition comprising mycobacterial DNA (*M. phlei* DNA) or mycobacterial cell wall complex (*M. phlei* cell wall complex) with a pharmaceutically acceptable carrier, and a chemotherapeutic agent. Claims 33-64 are currently pending. Claims 33, 41, 49, and 57 have been amended. Support for the amendments to the claims is found throughout the specification. No new matter has been added.

Election/Restriction Requirement

Applicants thank the Examiner for withdrawing the previously issued restriction requirement in light of the preliminary amendment filed by Applicants on April 15, 2002.

Rejection of Claims 33-64 under 35 U.S.C. §112, Paragraph 2

The Examiner rejects Claims 33-64 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and claim the subject matter that Applicants regard as the invention. Specifically, the Examiner rejects independent Claims 33, 41, 49, and 57 (and all claims dependent therefrom) asserting that it is unclear if the method of treatment in Claims 33, 41, 49, and 57 includes administering a chemotherapeutic agent in addition to the composition recited in the claims. Claims 33, 41, 49, and 57 are amended to recite that the method of treatment comprising: (1) administration of a pharmaceutical composition comprising *M. phlei* DNA or *M. phlei* cell wall complex and a pharmaceutically acceptable carrier, and (2) administration of a chemotherapeutic agent.

The Examiner further states that Claims 33, 41, 49, and 57 (and dependent Claims 34-40, 42-48, 50-56, and 58-63) are indefinite because they recite the phrase, "wherein the composition and a chemotherapeutic agent administered to the animal having cancer display an anti-cancer

synergism." According to the Examiner, the specification does not clearly define the term "synergism." Applicants respectfully assert that the term is clearly defined in the specification. At page 6, lines 7-8, Applicants state that "'synergism' relates to the coordinated action of two or more chemotherapeutic agents."

The Examiner further states that the rejected claims are vague because the specification does not clearly define "coordinated action," which is used to define synergism. In reviewing a claim for compliance with 35 U.S.C. § 112, second paragraph, the Examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and serves the notice function required by the statute. *See* MPEP § 2173.02 (citing *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379 (Fed. Cir. 2000)). If the claim at issue apprises one of ordinary skill in the art of its scope and provides notice, a rejection under 35 U.S.C. § 112, second paragraph is inappropriate. *See* MPEP § 2173.02 (citing *In re Larsen*, No. 01-1092 (Fed. Cir. May 9, 2001)).

The term "synergism" is commonly used and known in the art. Because "synergism" is a common term, the rejected claims would certainly apprise one of ordinary skill in the art of their scope and would provide notice. It is appropriate to compare the meaning of terms given in technical dictionaries to ascertain the accepted meaning of a term in the art. *See* MPEP § 2173.05 (b) (citing *In re Barr*, 444 F.2d 588 (CCPA 1971)). Merriam Webster Medical Dictionary defines "synergism" as the interaction of discrete agents (as drugs) such that the total effect is greater than the sum of the individual effects. *See* MERRIAM WEBSTER MEDICAL DICTIONARY (1997), available at http://www.intelihealth.com/IH/ihtIH/WSIHW000/9276/9276.html (last visited Aug. 13, 2002). Bantam Medical Dictionary defines "synergist" as a drug that interacts with another to produce increased activity that is greater than the sum of the effects of the two drugs given separately. *See* BANTAM MEDICAL DICTIONARY 423 (1990). Based on the accepted meaning of the term "synergism," one of ordinary skill in the art would understand that the rejected claims refer to increased anti-cancer activity as a result of coordinated action of the claimed composition and a chemotherapeutic agent.

The Examiner also rejects Claims 33 and 49 (and all claims dependent therefrom) as indefinite because they recite the phrase, " a composition comprising mycobacterial DNA complexed on mycobacterial cell wall (BCC)." The Examiner cites page 9, Examples 1 and 2 of

the specification stating that it is unclear how the DNA is complexed on the cell wall because the specification does not fully disclose any method to complex mycobacterial DNA to a cell wall. At page 9, Examples 1 and 2, Applicants describe the preparation of mycobacterial cell wall complex by incorporating by reference International Patent Application PCT/CA98/00744, which fully describes the method of preparing mycobacterial cell wall complex at page 12, Example 1. Applicants respectfully request withdrawal of the rejection of Claims 33-64 under 35 U.S.C. § 112, second paragraph in light of the foregoing amendments and remarks.

Rejection of Claims 33, 35, 37, 41, 43, 45, 49, 51, 53, 56, 57, 59, 61, and 64 under 35 U.S.C. § 102 (b)

The Examiner rejects Claims 33, 35, 37, 41, 43, 45, 49, 51, 53, 56, 57, 59, and 61 under 35 U.S.C. § 102 (b) as anticipated by Morales et al., 1995 (hereinafter *Morales*). The Examiner states that the rejection is appropriate because it is unclear if the claims are drawn to a method comprising administering a composition in a pharmaceutically acceptable carrier and a chemotherapeutic agent. Applicants have amended the claims to recite a method comprising administering a composition comprising M-DNA, B-DNA, MCC, or BCC in a pharmaceutically acceptable carrier and administering a chemotherapeutic agent. *Morales* does not teach the composition recited by the amended claims. In view of the foregoing amendments, Applicants respectfully request that the rejection of Claims 33, 35, 37, 41, 43, 45, 49, 51, 53, 56, 57, 59, 61, and 64 under 35 U.S.C. § 102(b) be withdrawn.

Rejection of Claims 33, 35-37, 41, 43-45, 49, 51-53, 56, 57, 59-61, and 64 under 35 U.S.C. § 103 (a)

The Examiner rejects Claims 33, 35-37, 41, 43-45, 49, 51-53, 56, 57, 59-61, and 64 under 35 U.S.C. § 103 (a) as being unpatentable over Morales et al. (hereinafter *Morales*) in view of Filion et al. (abstract 3476) (hereinafter *Filion*) and further in view of Filion et al. (abstract 2959) (hereinafter *Filion*). The Examiner states that the rejection is appropriate because it is unclear if the claims are drawn to a method comprising administering a composition in a pharmaceutically acceptable carrier and a chemotherapeutic agent. Applicants have amended the claims to clearly recite a method comprising administering a composition comprising M-DNA, B-DNA, MCC, or

BCC in a pharmaceutically acceptable carrier and administering a chemotherapeutic agent. Therefore, Applicants respectfully submit that the rejection is not appropriate in light of the amended claims. None of the references cited by the Examiner, alone or in combination, teaches or suggests Applicants' claimed method of treating cancer by administering the recited compositions in a pharmaceutically acceptable carrier and administering a chemotherapeutic agent. Therefore, Applicants respectfully request that the rejection of Claims 33, 35-37, 41, 43-45, 49, 51-53, 57, 59-61, and 64 under 35 U.S.C. § 103 (a) be withdrawn.

Version of Claim Amendments with Markings to Show Changes

33. (Amended) A method of treating cancer comprising:

(a) administration of a composition comprising *Mycobacterium phlei* (*M.phlei*)-DNA complexed on *Mycobacterium phlei* cell wall (MCC) and a pharmaceutically acceptable carrier; and

(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and [a] the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

41. (Amended) A method of treating cancer comprising:

(a) administration of a composition comprising *Mycobacterium phlei* (*M.phlei*)-DNA (M-DNA) and a pharmaceutically acceptable carrier; and

(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and [a] the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

49. (Amended) A method of treating cancer comprising:

(a) administration of a composition comprising a mycobacterial DNA complexed on mycobacterial cell wall (BCC), and a pharmaceutically acceptable carrier; and

(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and [a] the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

57. (Amended) A method of treating cancer comprising:

(a) administration of a composition comprising a mycobacterial DNA (B-DNA), and a pharmaceutically acceptable carrier; and

(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and [a] the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

Conclusion

In light of the amendments and the above remarks, Applicants are of the opinion that all Claims 33-64 are now in condition for allowance. Applicants further submit that present claims are not anticipated over the art of record, and earnestly solicit an early and favorable notice of allowability.

Should the Examiner believe that anything further is necessary to place the application in better condition for allowance, the Examiner is respectfully requested to contact Applicants' representative at the telephone number listed below.

No additional fees are currently believed due; however, please charge any additional fees or credit any overpayment to Deposit Account No. 11-0855.

Respectfully submitted,

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Currently Pending Claims

33. (Amended) A method of treating cancer comprising:

(a) administration of a composition comprising *Mycobacterium phlei* (*M.phlei*)-DNA complexed on *Mycobacterium phlei* cell wall (MCC) and a pharmaceutically acceptable carrier; and

(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

34. The method of Claim 33, wherein the anti-cancer synergism is potentiation.

35. The method of Claim 33, wherein the composition induces cell cycle arrest in cells of the cancer, inhibits proliferation of cells of the cancer, induces apoptosis in cells of the cancer, or synchronizes cell cycles of cells of the cancer.

36. The method of Claim 33, wherein the cancer is leukemia, lymphoma or melanoma.

37. The method of Claim 33, wherein cells of the cancer display resistance against one or more chemotherapeutic agents.

38. The method of Claim 33, wherein the chemotherapeutic agent is administered before, after, or concurrently with the administration of the composition.

39. The method of Claim 33, wherein the chemotherapeutic agent is a DNA cross-linking agent, a DNA depolymerizing agent, an antimetabolic agent, an anti-tumor antibiotic agent, a topoisomerase inhibiting agent or a tubulin stabilizing agent.

40. The method of Claim 33, wherein the chemotherapeutic agent is mitomycin-C, 5-fluorouracil, or cisplatin.

41. (Amended) A method of treating cancer comprising:

(a) administration of a composition comprising *Mycobacterium phlei* (*M.phlei*)-DNA (M-DNA) and a pharmaceutically acceptable carrier; and

(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

42. The method of Claim 41, wherein the anti-cancer synergism is potentiation.

43. The method of Claim 41, wherein the composition induces cell cycle arrest in cells of the cancer, inhibits proliferation of cells of the cancer, induces apoptosis in cells of the cancer, or synchronizes cell cycles of cells of the cancer.

44. The method of Claim 41, wherein the cancer is leukemia, lymphoma or melanoma.

45. The method of Claim 41, wherein cells of the cancer display resistance against one or more chemotherapeutic agents.

46. The method of Claim 41, wherein the chemotherapeutic agent is administered before, after, or concurrently with the administration of the composition.

47. The method of Claim 41, wherein the chemotherapeutic agent is a DNA cross-linking agent, a DNA depolymerizing agent, an antimetabolic agent, an anti-tumor antibiotic agent, a topoisomerase inhibiting agent or a tubulin stabilizing agent.

48. The method of Claim 41, wherein the chemotherapeutic agent is mitomycin-C, 5-fluorouracil, or cisplatin.

49. (Amended) A method of treating cancer comprising:

(a) administration of a composition comprising a mycobacterial DNA complexed on mycobacterial cell wall (BCC), and a pharmaceutically acceptable carrier; and

(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and [a] the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

50. The method of Claim 49, wherein the anti-cancer synergism is potentiation.

51. The method of Claim 49, wherein the composition induces cell cycle arrest in cells of the cancer, inhibits proliferation of cells of the cancer, induces apoptosis in cells of the cancer, or synchronizes cell cycles of cells of the cancer.

52. The method of Claim 49, wherein the cancer is leukemia, lymphoma or melanoma.

53. The method of Claim 49, wherein cells of the cancer display resistance against one or more chemotherapeutic agents.

54. The method of Claim 49, wherein the chemotherapeutic agent is administered before, after, or concurrently with the administration of the composition.

55. The method of Claim 49, wherein the chemotherapeutic agent is a DNA cross-linking agent, a DNA depolymerizing agent, an antimetabolic agent, an anti-tumor antibiotic agent, a topoisomerase inhibiting agent or a tubulin stabilizing agent.

56. The method of Claim 49, wherein BCC is derived from *M. vaccae, M. chelonei, M. smegmatis, M. terrae, M. duvalii, M. tuberculosis, M. bovis BCG, M. avium, M. Szulgai, M. scrofulaceum, M. xenopi, M. kansaii, M. gastr, M. fortuitous,* or *M. asiaticum.*

57. (Amended) A method of treating cancer comprising:

(a) administration of a composition comprising a mycobacterial DNA (B-DNA), and a pharmaceutically acceptable carrier; and

(b) administration of a chemotherapeutic agent to an animal or a human having cancer, wherein the composition and [a] the chemotherapeutic agent administered to the animal or the human having cancer display an anti-cancer synergism.

58. The method of Claim 57, wherein the anti-cancer synergism is potentiation.

59. The method of Claim 57, wherein the composition induces cell cycle arrest in cells of the cancer, inhibits proliferation of cells of the cancer, induces apoptosis in cells of the cancer, or synchronizes cell cycles of cells of the cancer.

60. The method of Claim 57, wherein the cancer is leukemia, lymphoma or melanoma.

61. The method of Claim 57, wherein cells of the cancer display resistance against one or more chemotherapeutic agents.

62. The method of Claim 57, wherein the chemotherapeutic agent is administered before, after, or concurrently with the administration of the composition.

63. The method of Claim 57, wherein the chemotherapeutic agent is a DNA cross-linking agent, a DNA depolymerizing agent, an antimetabolic agent, an anti-tumor antibiotic agent, a topoisomerase inhibiting agent or a tubulin stabilizing agent.

64. The method of Claim 57, wherein B-DNA is derived from *M. vaccae, M. chelonei, M. smegmatis, M. terrae, M. duvalii, M. tuberculosis, M. bovis BCG, M. avium, M. Szulgai, M. scrofulaceum, M. xenopi, M. kansaii, M. gastr, M. fortuitous,* or *M. asiaticum*.